UNIVERSITÀ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

TURIN
October
24th-26th
2019

31 GIORNATE CARDIOLOGICHE TORINESI

Everything you always wanted to know about
Cardiovascular Medicine

Recurrent VTs in structural heart disease: the role of neuromodulation

Torino, 25 ottobre 2019

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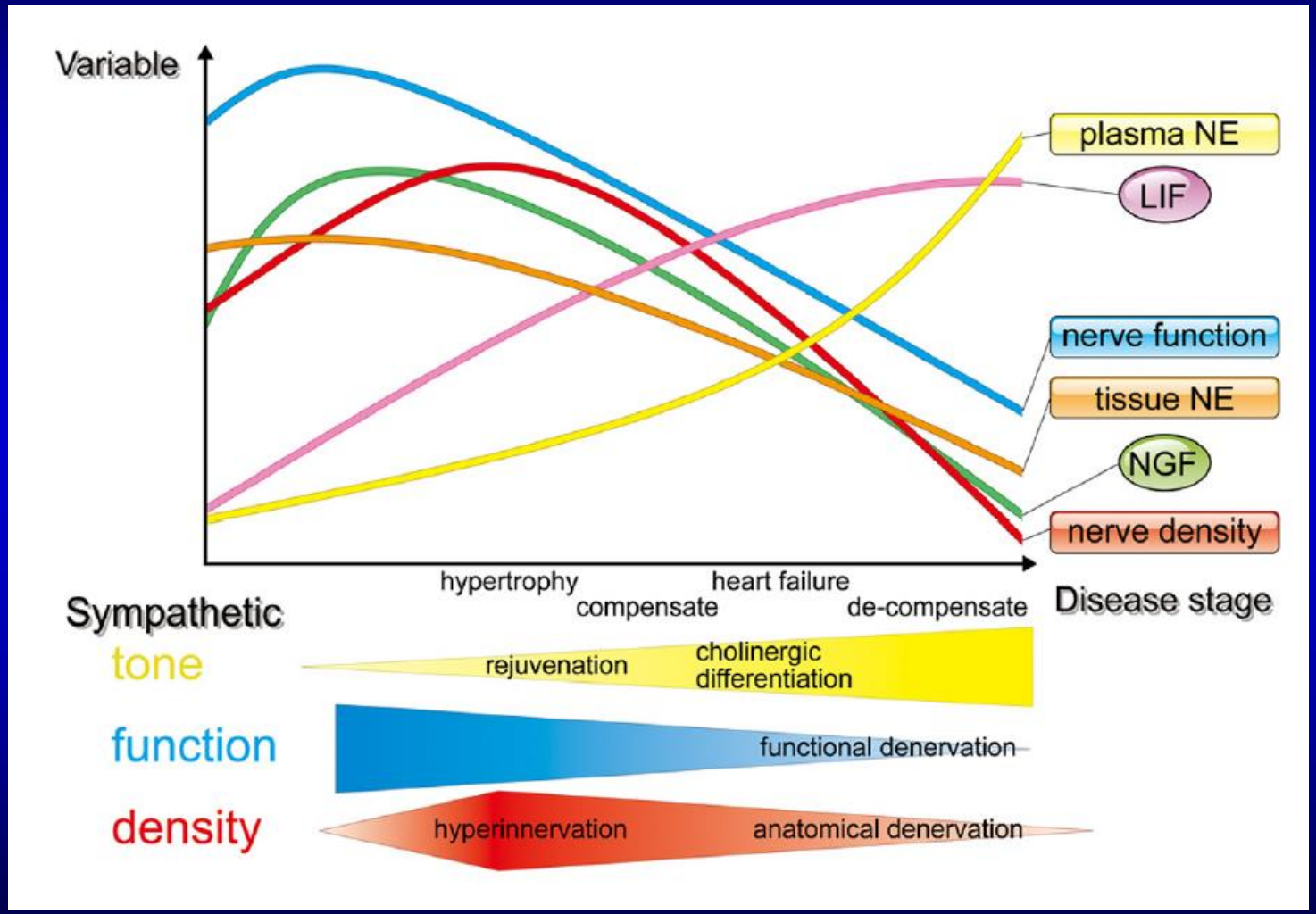
Policlinico San Matteo, Pavia

Temporal Changes in Cardiac Innervation With Disease Progression



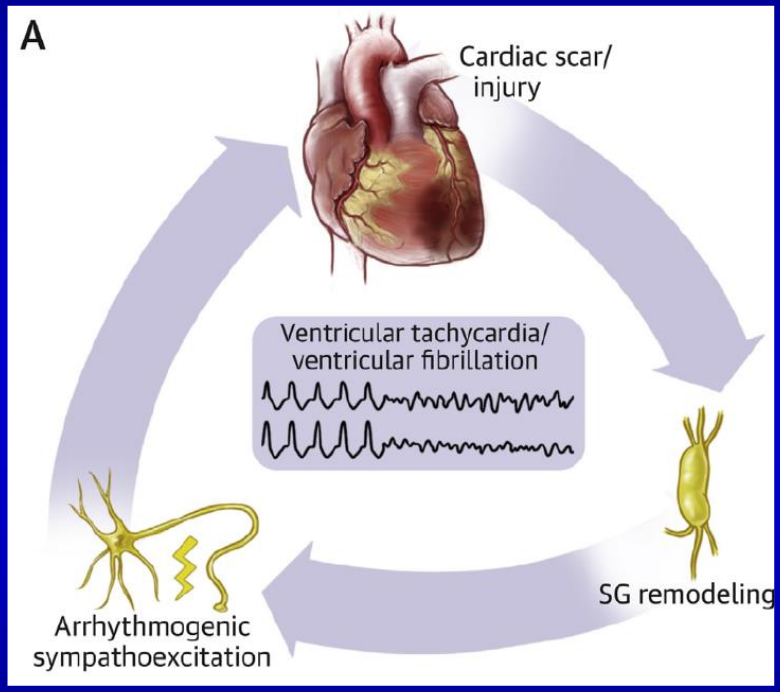
Fukuda et al. Circ Res. 2015;116:2005-19

Arrhythmogenic Effects of Sympathetic Hyperactivity/Remodeling

- Increased impulse formation (EADs and DADs)
- Shortened refractoriness
- Increased spatial and temporal dispersion of refractoriness
- Increased directionally dependent impulse propagation
- EADs facilitated re-entry

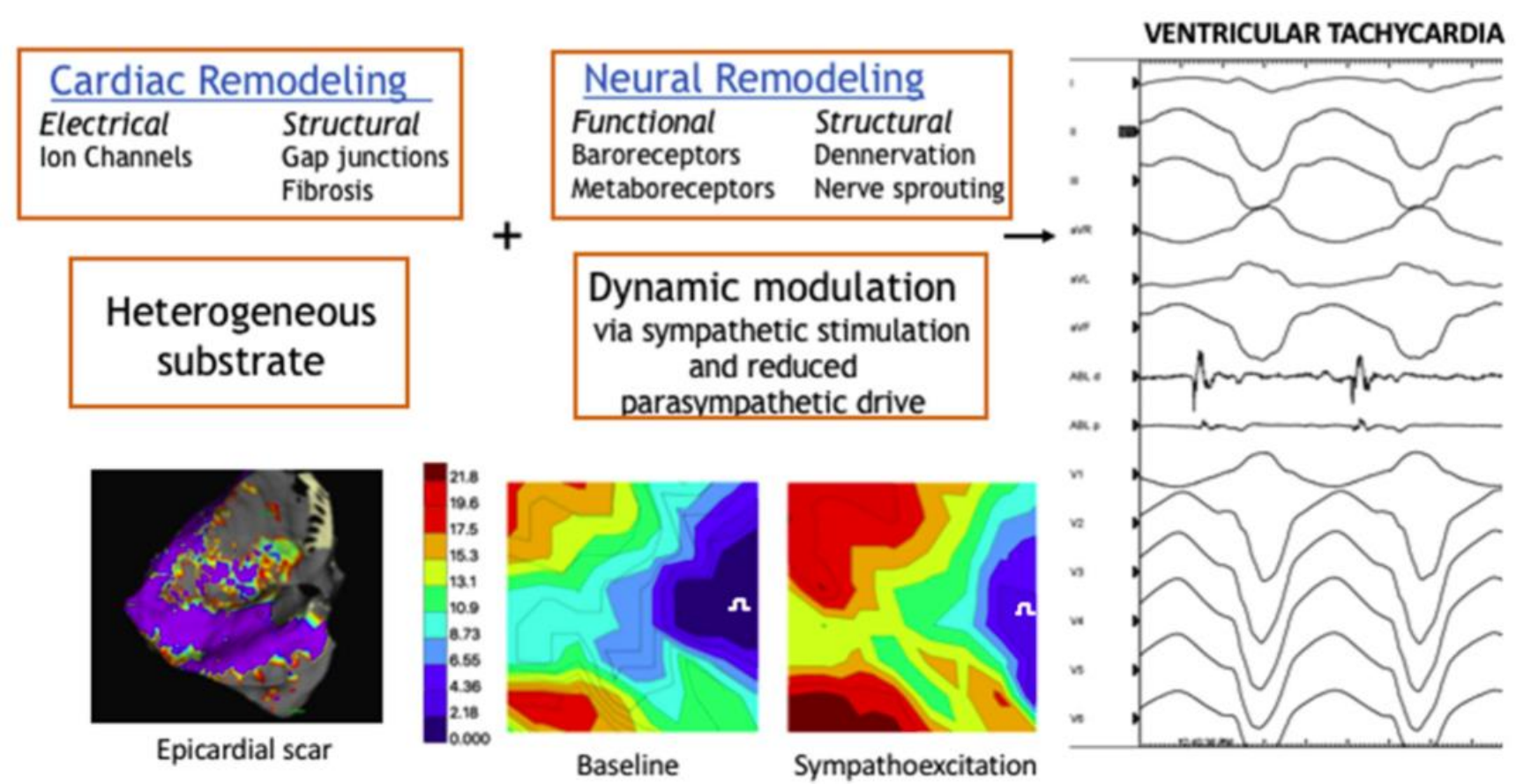
- HR rise+VO_2 rise increase ischemic and EP changes
- HR rise increases likelihood of conduction blocks

- Denervation and reinnervation are heterogeneous and dynamic processes



J Am Coll Cardiol EP 2019; 5: 881

VTs in SHD: a unifying framework



Bradfield JS et al. Hearth Rhythm 2018; 15 (8)

Three-Dimensional ^{123}I-*Meta*-Iodobenzylguanidine Cardiac Innervation Maps to Assess Substrate and Successful Ablation Sites for Ventricular Tachycardia

Feasibility Study for a Novel Paradigm of Innervation Imaging

Thomas Klein, MD; Mohammed Abdulghani, MD; Mark Smith, PhD; Rui Huang, MD; Ramazan Asoglu, MD; Benjamin F. Remo, MD; Aharon Turgeman, MSc, MBA; Olurotimi Mesubi, MD; Sunjeet Sidhu, MD; Stephen Synowski, PhD; Anastasios Saliaris, MD; Vincent See, MD; Stephen Shorofsky, MD, PhD; Wengen Chen, MD, PhD; Vasken Dilsizian, MD; Timm Dickfeld, MD, PhD

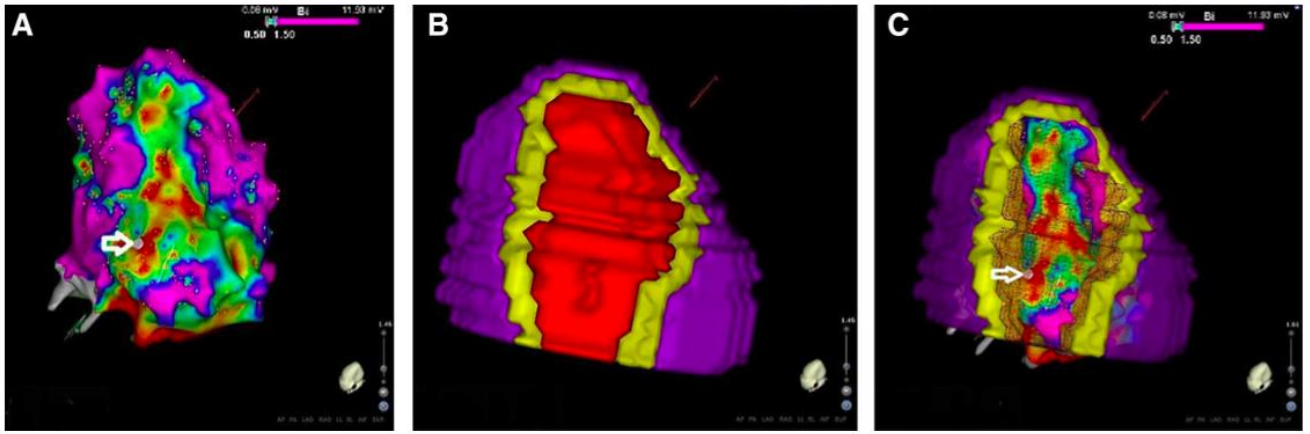
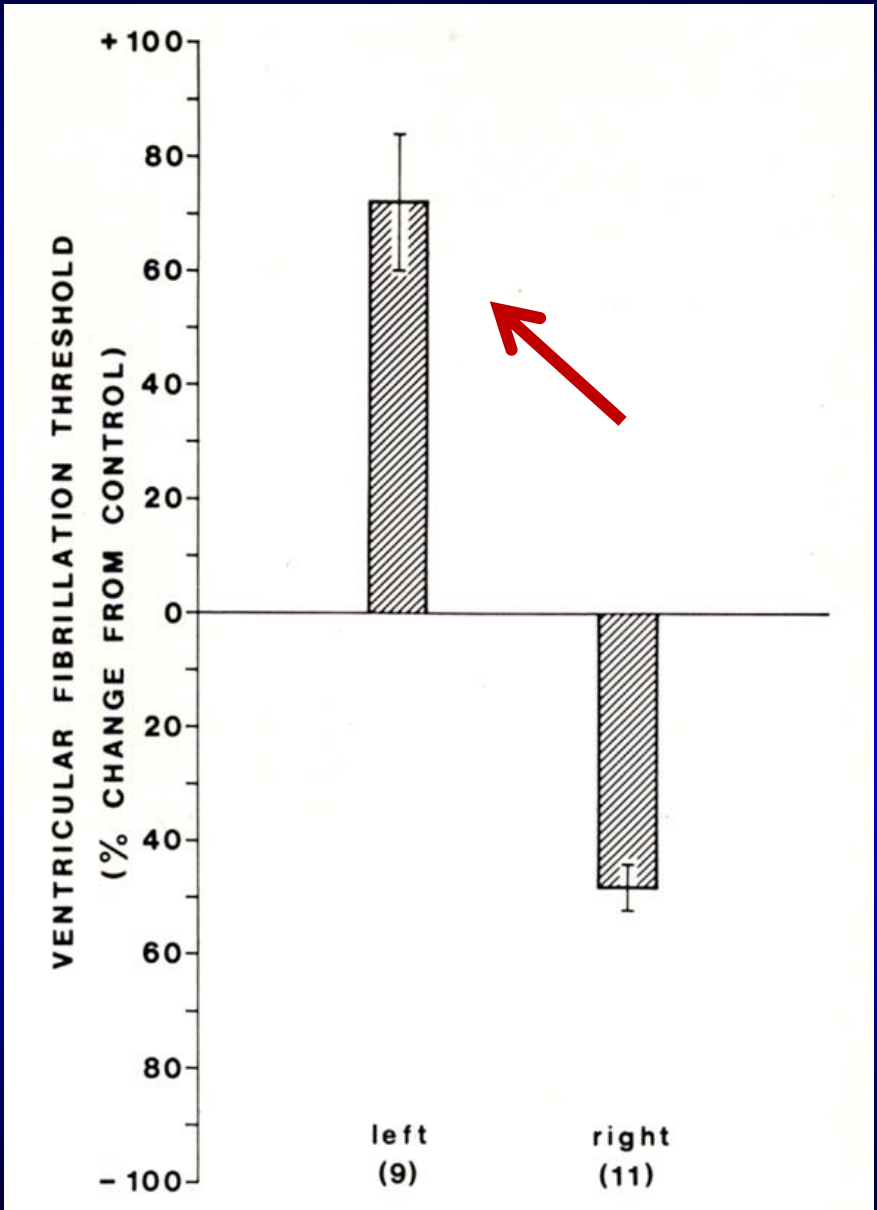


Figure 5. Comparison of 3-dimensional innervation map and electroanatomic map. Concordant voltage scar-denervation location of successful ablation site. **A**, Bipolar electroanatomic map, inferior view, demonstrating inferior scar (red) and border zone (yellow-blue) with successful ablation site (white dot; white arrow) within scar. **B**, Reconstructed ^{123}I-*meta*iodobenzylguanidine scar map, inferior view, demonstrating regional denervation in the inferior wall (denervated myocardium in red, transition zone in yellow, and normally innervated myocardium in purple). **C**, Coregistration of electroanatomic map and innervation map demonstrates that area of denervation (red transparent mesh) extends beyond the area of bipolar scar (and border zone). Successful ablation site (white dot; white arrow) is located in area of voltage-defined scar (as shown in **A**), but also in the area of myocardial denervation close to the interface of denervation (red mesh) and neuronal transition zone (nontransparent yellow).

Conclusions—^{123}I-*m*IBG innervation defects are larger than bipolar voltage–defined scar and cannot be detected with standard voltage criteria. Thirty-six percent of successful VT ablation sites demonstrated normal voltages (>1.5 mV), but all ablation sites were within the areas of abnormal innervation. ^{123}I-*m*IBG innervation maps may provide critical information about triggers/substrate modifiers and could improve understanding of VT substrate and facilitate VT ablation.

Circ Arrhythm Electrophysiol. 2015;8:583-91

Stellate Ganglion Block and VFT

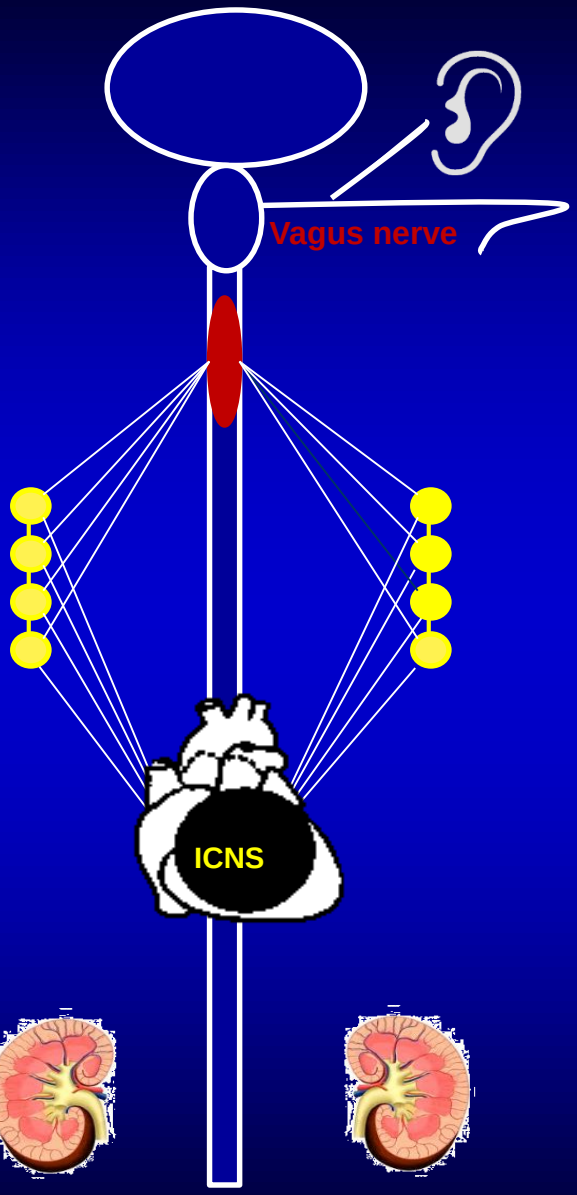


PJ Schwartz et al, Am J Cardiol 1976

NEURAXIAL LEVEL

ANTIARRHYTHMIC INTERVENTION

Brainstem and higher centers



Thoracic T1-T4 spinal cord

Thoracic sympathetic chain and ganglia T1-T4

Intrinsic cardiac nervous system

Renal artery sympathetic fibers

Electrical vagal stimulation

- Auricular Branch of the Vagus Nerve Stimulation
- Cervical Vagal Nerve Stimulation

Spinal cord interventions

- Thoracic Epidural Anesthesia
- Spinal Cord Stimulation

Interventions on Stellate ganglion/sympathetic chain

- Percutaneous stellate Ganglion Block
- Stellate Ganglion Radiofrequency Ablation
- Cardiac Sympathetic Denervation (cervicothoracic sympathectomy)

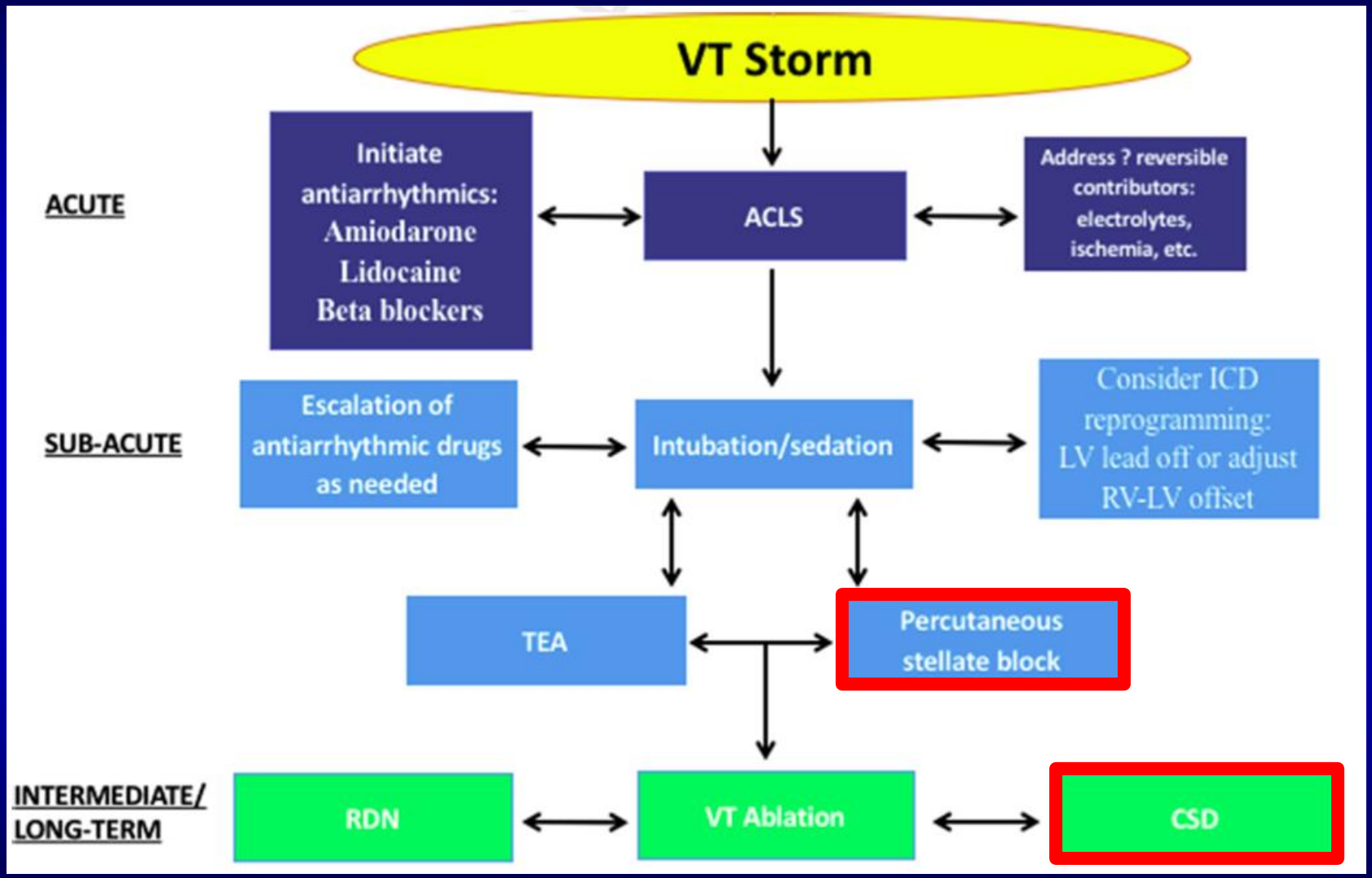
Interventions on ICNS

- Ganglionated Plexi Ablation
- Botulinum Toxin Injection

- Renal Denervation

Modified from V. Dusi et al, Curr Cardiol Rep. 2019;18:32

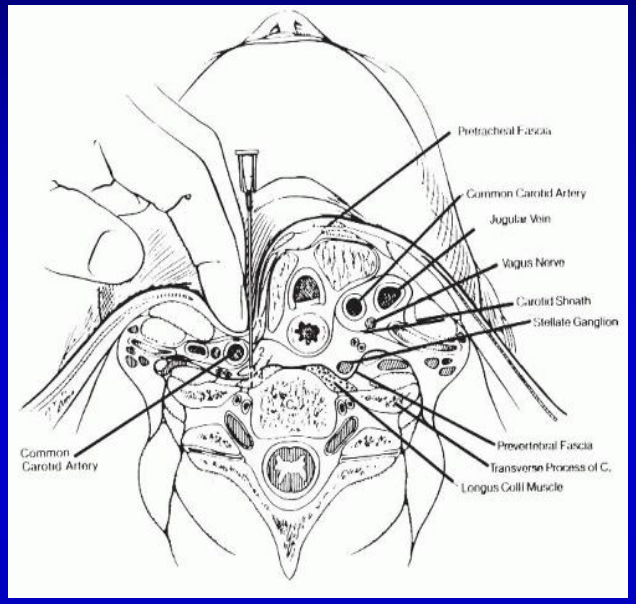
The UCLA's approach



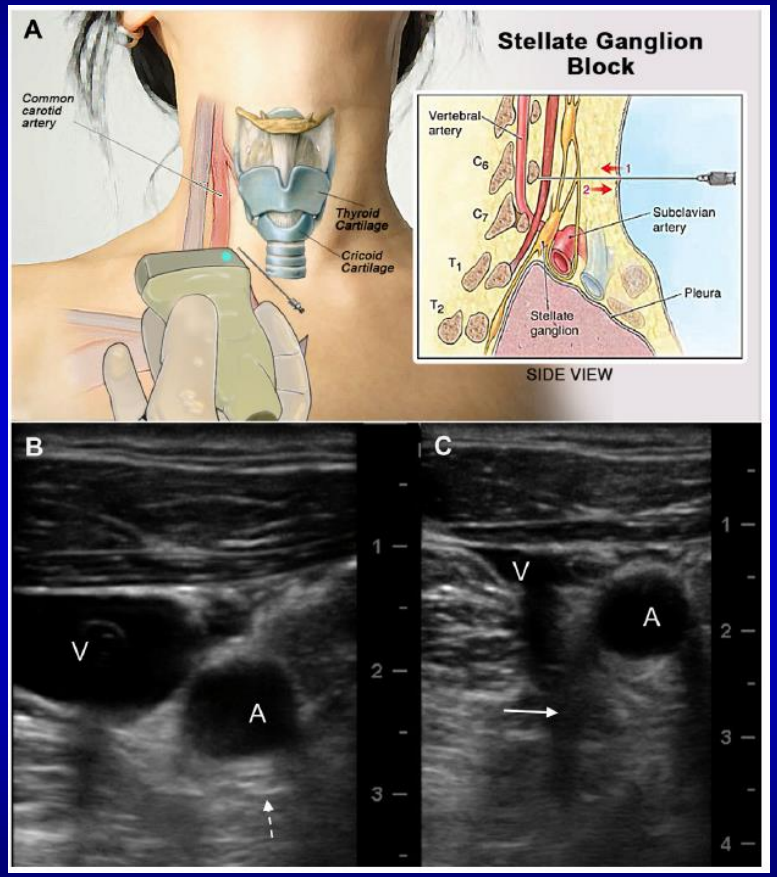
Bradfield JS et al. Hearth Rhythm 2018; 15 (8)

Percutaneous stellate ganglion block (PSGB)

Anatomical approach



US-guided approach



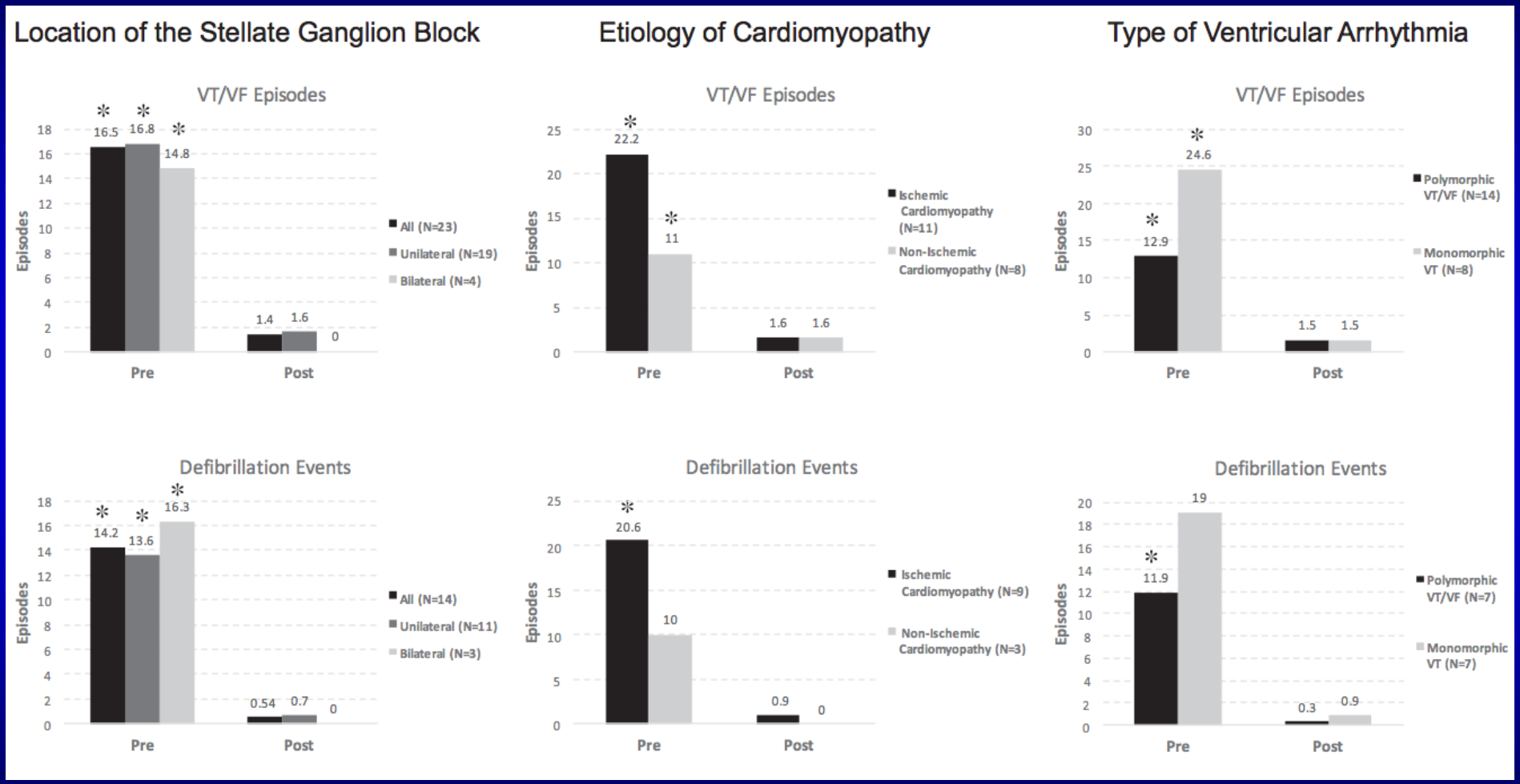
Pros:

- Can be safely performed at bedside by a trained cardiologist
- Trivial infective and hemorrhagic risk

Cons:

- Not quantifiable ipsilateral neuronal sympathetic block at cardiac level

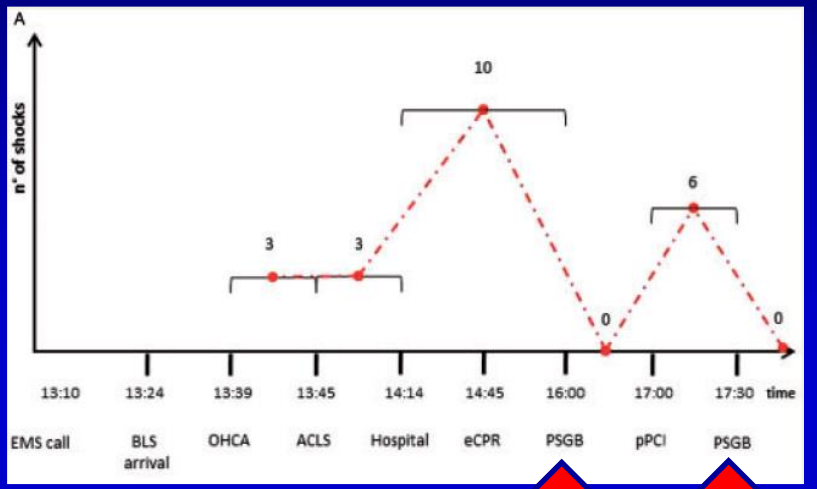
Arrhythmic burden 24 ore pre vs post PSGB

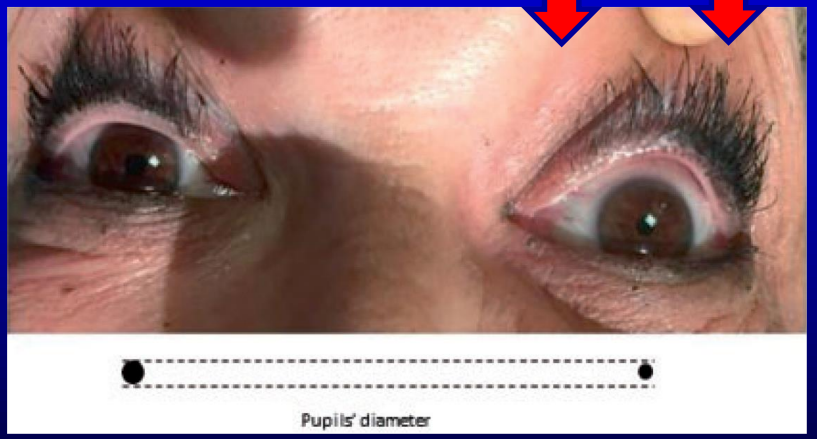


Fudimi M et al. J Cardiovasc Electrophysiol.2017;1–8

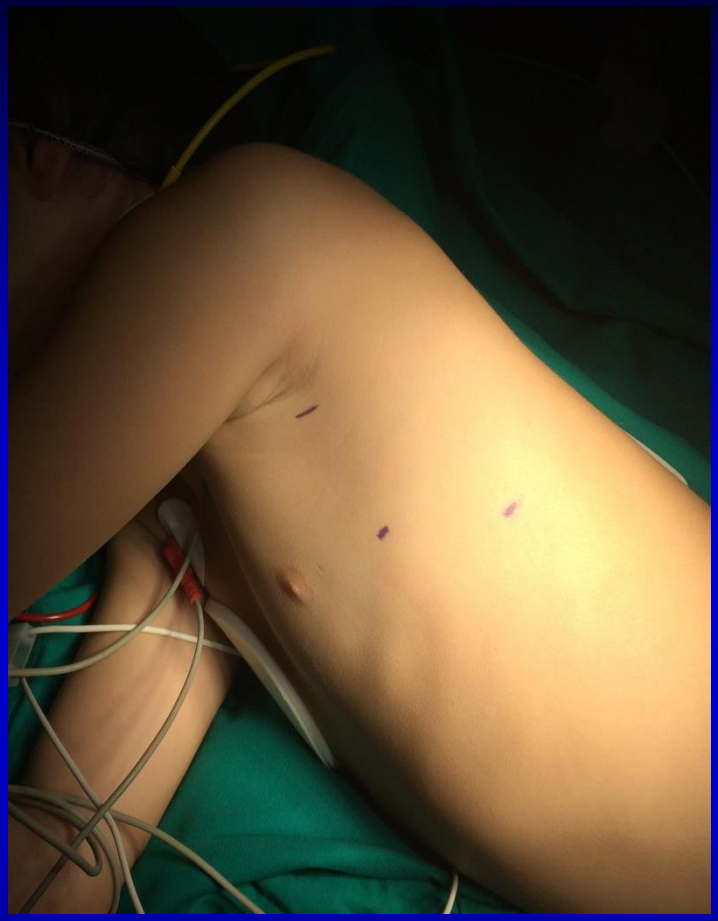
PSGB in Pavia

- First Italian Center to report about PSGB to treat ES/refractory VT/VF
- A prospective study of PSGB in patients with refractory ES was started on July 2017 (PI Savastano Simone)
- 17 left PSGBs (2 during ECMO) have been performed so far (including 2 continuous infusion as a bridge to CSD)
- A training course is now offered to internal and external cardiologist and anesthesiologist willing to learn the procedure



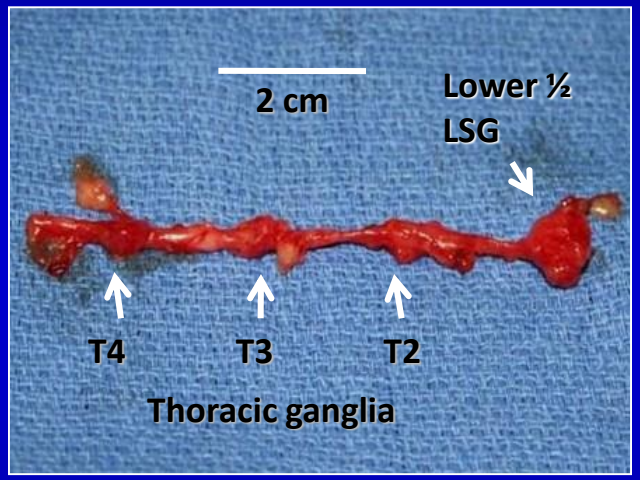


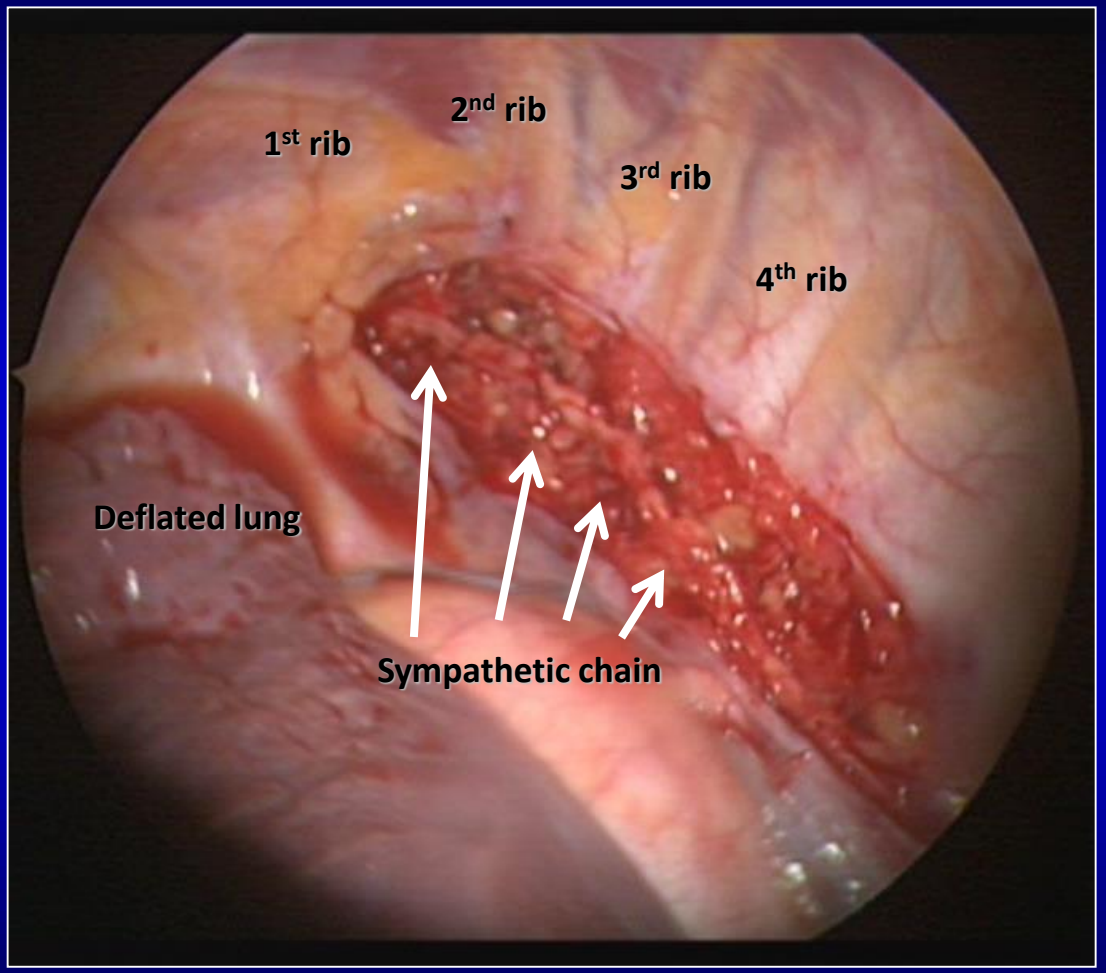
Savastano S, Baldi E, et al. Europace. 2019, doi: 10.1093/europace/euz180



VATS-CSD

Anatomy of left sympathetic chain





Bourke T, et al. Circulation. 2010;121(21):2255-2262

Left Cardiac Sympathetic Denervation in the Management of High-Risk Patients Affected by the Long-QT Syndrome

Peter J. Schwartz, MD; Silvia G. Priori, MD, PhD; Marina Cerrone, MD; Carla Spazzolini, PhD; Attilio Odero, MD; Carlo Napolitano, MD, PhD; Raffaella Bloise, MD; Gaetano M. De Ferrari, MD; Catherine Klersy, MD, MS; Arthur J. Moss, MD; Wojciech Zareba, MD; Jennifer L. Robinson, MS; W. Jackson Hall, PhD; Paul A. Brink, MD; Lauri Toivonen, MD; Andrew E. Epstein, MD; Cuilan Li, MD; Dayi Hu, MD

(*Circulation*. 2004;109:1826-1833.)

LQTS
- 2015 ESC GL: Class IIa indication
- 2017 AHA/ACC/HRS GL: Class I for symptoms
- 2017 AHA/ACC/HRS GL: Class IIb for asymptom

Clinical Management of Catecholaminergic Polymorphic Ventricular Tachycardia

The Role of Left Cardiac Sympathetic Denervation

Gaetano M. De Ferrari, MD*; Veronica Dusi, MD*; Carla Spazzolini, DVM, MS*; J. Martijn Bos, MD, PhD*; Dominic J. Abrams, MD, MRCP; Charles I. Berul, MD; Lia Crotti, MD, PhD; Andrew M. Davis, MB, BS, MD; Michael Eldar, MD; Maria Kharlap, MD; Asaad Khoury, MD; Andrew D. Krahn, MD; Antoine Leenhardt, MD; Christopher R. Moir, MD; Attilio Odero, MD; Louise Olde Nordkamp, MD; Thomas Paul, MD; Ferran Rosés i Noguer, MD; Maria Shkolnikova, MD; Jan Till, MD; Arthur A.M. Wilde, MD; Michael J. Ackerman, MD, PhD†; Peter J. Schwartz, MD†

Circulation. 2015;131:2185-2193

CPVT
- 2015 ESC GL: Class IIb indication
- 2017 AHA/ACC/HRS: Class I for symptoms

Mar 2014

Single center Study (UCLA)

Cardiac sympathetic denervation in patients with refractory ventricular arrhythmias or electrical storm: Intermediate and long-term follow-up

Marmar Vaseghi, MD, MS,* Jean Gima, RN, MSN, NP,* Christopher Kanaan, BS,* Olujimi A. Ajijola, MD, PhD,* Alexander Marmureanu, MD,*† Aman Mahajan, MD, PhD,*‡ Kalyanam Shivkumar, MD, PhD, FHRS*

*From the *UCLA Cardiac Arrhythmia Center, †Division of Cardiothoracic Surgery, and ‡Department of Anesthesiology, UCLA Health System, Los Angeles, California.*

n=41, 34% LCSD, LVEF 31± 13%, **80% with MMVT**

June 2017

Multicenter Study (n=5)

Cardiac Sympathetic Denervation for Refractory Ventricular Arrhythmias

Marmar Vaseghi, MD, PhD,[a,b] Parag Barwad, MD, DM,[c] Federico J. Malavassi Corrales, MD,[d] Harikrishna Tandri, MD, MBBS,[e] Nilesh Mathuria, MD,[f] Rushil Shah, MBBS,[c] Julie M. Sorg, RN, MSN,[a] Jean Gima, RN, MSN, NP,[a] Kaushik Mandal, MD, MBBS,[e] Luis C. Sàenz Morales, MD,[d] Yash Lokhandwala, MD, DM,[c] Kalyanam Shivkumar, MD, PhD[a,b]

n=121, 19% LCSD, LVEF 30±12%, 71% NICM

71% with MMVT, 64% >1 VT morphology

66% previous VT ablation, median 2/pt (IQR 1-2)

2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

5.6. Autonomic Modulation

Recommendations for Autonomic Modulation

References that support the recommendations are summarized in Online Data Supplement 13 and 14.

COR	LOE	Recommendations
IIa	C-LD	1. In patients with symptomatic, non–life-threatening VA, treatment with a beta blocker is reasonable (1).
IIb	C-LD	2. In patients with VT/VF storm in whom a beta blocker, other antiarrhythmic medications, and catheter ablation are ineffective, not tolerated, or not possible, cardiac sympathetic denervation may be reasonable (2-4).

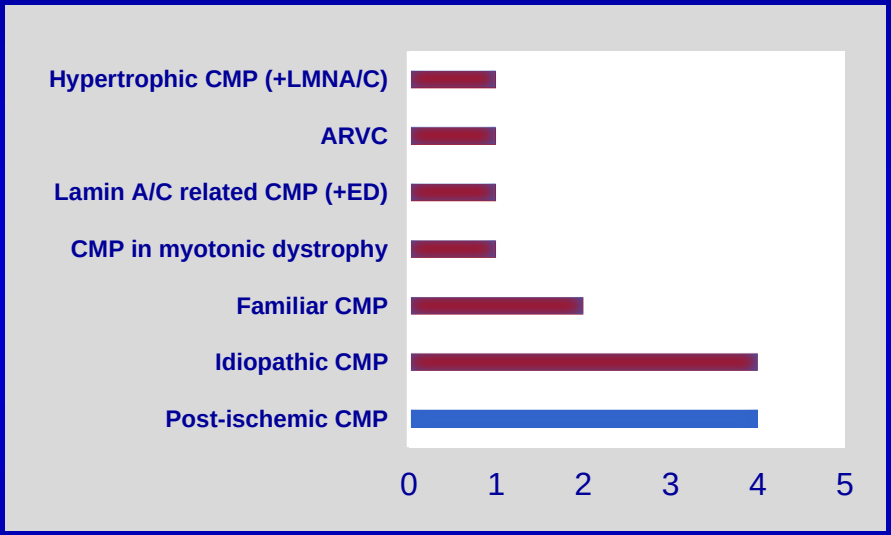
2. Vaseghi M, et al.Cardiac sympathetic denervation for refractory ventricular arrhythmias. J Am Coll Cardiol. 2017;69:3070-80.

3. Vaseghi M, et al.Cardiac sympathetic denervation in patients with refractory ventricular arrhythmias or electrical storm: intermediate and long-term follow-up. HeartRhythm.2014;11:360-6.

4. Schwartz PJ, et al. Prevention of sudden cardiac death after a first myocardial infarction by pharmacologic or surgical antiadrenergic interventions. JCardiovascElectrophysiol.1992;3:2-16.

BCSD in SHD: Pavia's experience

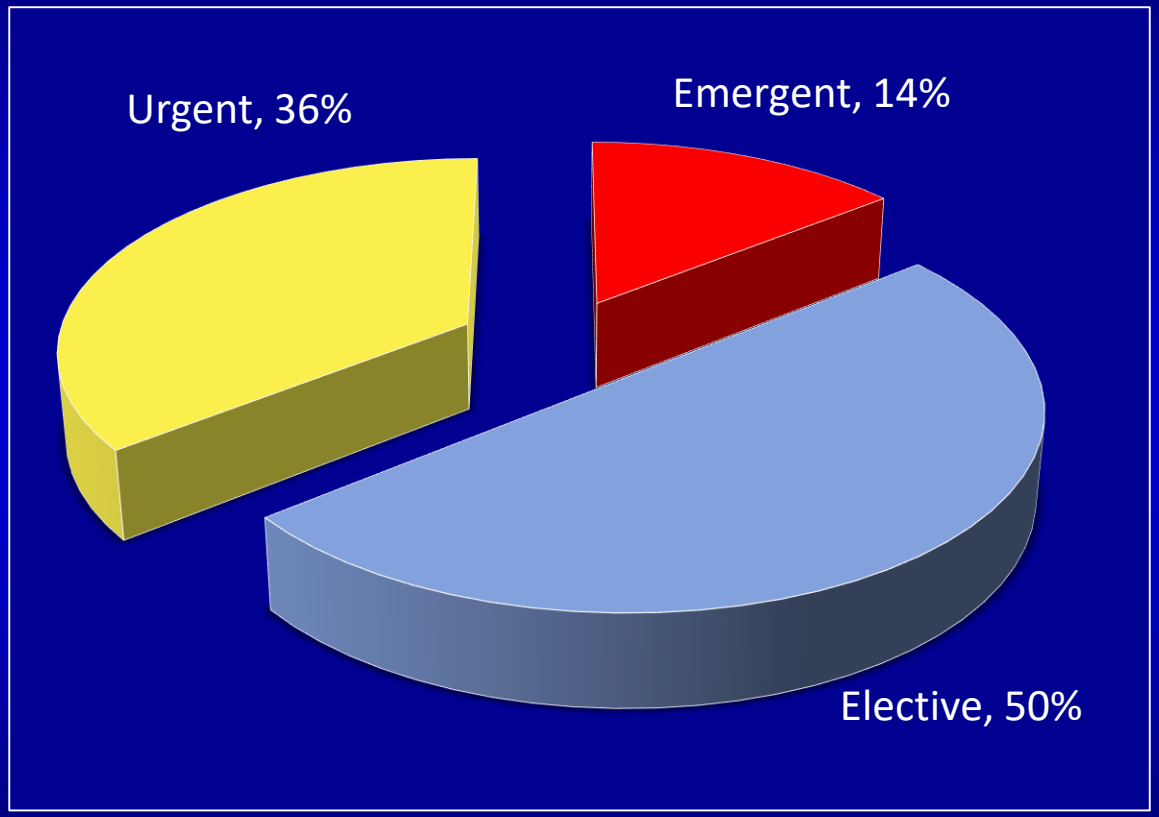
- First BCSD in SHD (VATS): April 2016

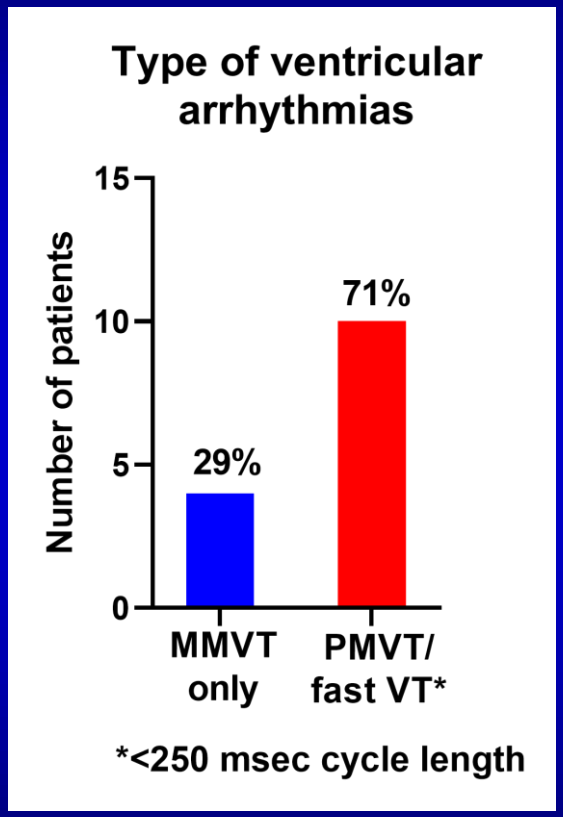


71% NICM

Baseline characteristics, N = 14	N, %
Male	12, 86%
Mean age	56 ± 16
Robotic VATS	2, 14%
ICD (transvenous)	13, 93%
CRT-D	5, 36%
History of AT/AF	6, 43%
LVEF (%)	31 ± 13
NYHA Class ≥ 3	4, 29%
VAD/OHT indication (for HF)	6, 43%
History of electrical storm	10, 71%
Chronic amiodarone	9, 64%
>1 chronic AAD	3, 21%
Previous VT/PVC ablation	5/1, 43%
Previous PLSGB	1, 7%

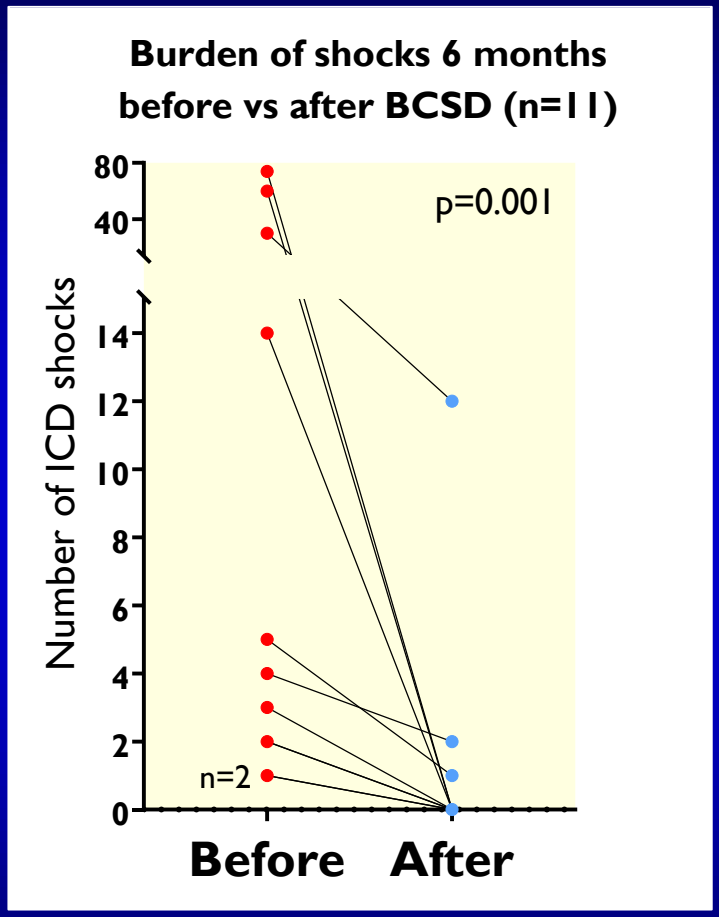
Indication/Presentation





Outcomes

- Median FU 12 months (IQR 6-23)
- Procedural related complications:
  - No major complications
  - 8 (57%) patients had transient post-operative neuropathic pain
- Hard events, n=3 (21%)
  - 1 Death due to refractory VAs in AHF (NYHA III, severe MR)
  - 1 LVAD implantation due to refractory VAs in AHF (NYHA III, severe MR, MMVT, Lamin A/C CMP)
  - 1 Heart transplantation (no VAs before)
- Incidence of VAs, total n=6 (43%) :
  - ICD shock: 5/14 (36%)
  - ATP only: 1/14 (7%)



Median 3 (2-22) versus 0 (0-0.5)

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